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Document Listing

Document	Selected Pages	Page Range	Copies
US006340478	14	1 - 14	1
US006149938	7	1 - 7	1
US005578307	10	1 - 10	1
US005401502	10	1 - 10	1
Total (4)	41	-	-

L16 ANSWER 46 OF 60 USPATFULL on STN

ACCESSION NUMBER:	2000:156993 USPATFULL
TITLE:	Process for the preparation of a granulate suitable to the preparation of rapidly disintegrable mouth-soluble tablets and compositions obtained thereby
INVENTOR(S):	Bonadeo, Daniele, Varese, Italy Ciccarello, Franco, Via la Loggia Mezzovico, Switzerland Pagano, Aberto, L'Aquila, Italy
PATENT ASSIGNEE(S):	Elan Pharma International Limited, Dublin, Ireland (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6149938		20001121	
APPLICATION INFO.:	US 1998-122037		19980723	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	CH 1997-1797	19970725

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Page, Thurman K.
ASSISTANT EXAMINER:	Berman, Alysia
LEGAL REPRESENTATIVE:	Anderson, Kirsten A.
NUMBER OF CLAIMS:	8
EXEMPLARY CLAIM:	1
LINE COUNT:	563

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . consisting of microcapsules containing th

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TRY' ENTERED AT 16:22:29 ON 09 JAN 2004
L1             0 S GINKO BILOBA/CN
L2             0 S GINKO BILOBA
L3             0 S GINCKO
L4             1 S PVP/CN
L5           208 S BILOBA
L6           189 S GINKGO BILOBA
L7             0 S GINKGO BILOBA/CN

     FILE 'USPATFULL, CAPLUS, KOSMET, IPA' ENTERED AT 16:24:31 ON 09 JAN 2004
L8         87445 S L4 OR (POLYVINYLPYRROLIDONE) OR (POLYVINYL PYRROLIDONE)
L9          3071 S L6 OR (GINKO BILOBA) OR (GINKGO BILOBA)
L10      1685777 S COAT#####
L11      2963746 S PELLET# OR CORE# OR POWDER## OR MICROGRANULE# OR GRANULE#
OR
L12            1 S L8 (20W) L9
L13          107 S L8 AND L9
L14           64 S L13 AND L10
L15           61 S L11 AND L14
L16           60 DUPLICATE REMOVE L15 (1 DUPLICATE REMOVED)
```

L16 ANSWER 43 OF 60 USPATFULL on STN
ACCESSION NUMBER: 2001:21762 USPATFULL
TITLE: **Ginkgo biloba** composition method to prepare the same and uses thereof
INVENTOR(S): Xie, De Long, Shanghai, China
Wang, Ning, Shanghai, China
Gao, Oi, Shanghai, China
Zhang, Guo An, Shanghai, China
Shao, Bao Ping, Shanghai, China
Jin, Xiao Wu, Shanghai, China
Huang, Xin Sheng, Shanghai, China
PATENT ASSIGNEE(S): Shanghai Inst. of Chinese Materia Medica, Shanghai, China (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6187314	B1	20010213
APPLICATION INFO.:	US 1998-97058		19980612 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-44551, filed on 19 Mar 1998, now patented, Pat. No. US 6030621
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Tate, Christopher
LEGAL REPRESENTATIVE: Chan, Albert Wai-Kit, Elkins, Mark
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 1379
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI **Ginkgo biloba** composition method to prepare the same and uses thereof

AB This invention provides different compositions extracted from **Ginkgo biloba** leaves. Said compositions comprise new active components. This invention also provides a method of preparation of the compositions and individual. . .

PARN This is a divisional application from the parent application entitled **Ginkgo Biloba** Composition, Method To Prepare The Same And Uses Thereof, application Ser. No. 09/044,551, filed on Mar. 19, 1998, now U.S.. . .

SUMM **Ginkgo Biloba** is the oldest genus among existing seed plants and the only survivor of the family Ginkgoaceae, that can be traced back more than 200 million years to the fossils of the Permian period. Preparations of **Ginkgo Biloba** leaves have been used as remedies in China for more than 5,000 years, I. e. since the earliest origin of Chinese herbal medicine. Phytopharmaceutical extracts from the leaves of **Ginkgo biloba** have been applied to treat cerebrovascular and peripheral vascular diseases in many countries, such as Germany, France, Japan and Korea. . .

SUMM The principal effective component in **Ginkgo biloba** leaves is flavonoids, that comprise at least 14 different compounds, such as flavonols, flavones, flavanols and biflavonoids etc. Among all. . . flavone glycosides and flavonol glycosides, that include kaempferol, quercetin and isorhamnetin with glucose or rhamnose, are the most emphasized in **Ginkgo biloba** extracts on the market for therapeutic purposes (Tebonin.RTM., Tanakan.RTM., Roekan.RTM., or "EGb 761"). As experiments have demonstrated, flavone glycosides and. . . Vol. 15 (1986), 1475-1479; J. Robak et al., Biochem Pharmacol Vol 37 (1988), 837-841 and J. Kleijnen and P.

Knipschild, **Ginkgo biloba** (Drug Profiles), the Lancet 340:1136 (1992). In addition, the flavone glycosides and flavonol glycosides increase peripheral circulation. Methods of preparation of **Ginkgo biloba** extracts with a greatly enriched content of flavone glycosides as the active components are described in DE-B 17 67 098 and DE-B 21 17 429. These preparations are **Ginkgo biloba** monoextracts.

SUMM Besides flavonoids, another major active constituent in **Ginkgo biloba** leaves is terpene lactones, that include ginkgolides A, B, C, J, M and bilobalide. Ginkgolides are terpenoid substances with lactone. . .

SUMM In addition to the compounds mentioned above, **Ginkgo biloba** leaves also contain at least 12 alkyl phenolic acid compounds including ginkgolic acids (anacardic acids) that are 6-alkylsalicylic acids with. . . (1968), 739-743. Structurally similar to the irritants in poison ivy, ginkgolic acids are the factors responsible for toxic effects of **Ginkgo biloba** extracts, that include gastrointestinal disturbances, headaches, skin irritation, dermatitis and edema. Many cases of allergic reactions after contact with **Ginkgo biloba** leaves or fruits have been reported since the 1960's; see G. A. Hill et al., J. Am. Chem. Soc., Vol.. . .

SUMM **Ginkgo biloba** extract used most frequently at present for therapeutic purposes (Tebonin.RTM., Tanakan.RTM., Roekan.RTM., or "EGb 76111") contains 24% flavone glycosides and. . . the ginkgolides A, B, C and J as well as the bilobalide, which makes up approximately half of the 6%. **Ginkgo biloba** extract normally contains less than 10 ppm (parts per million) alkylphenol compounds. The therapeutic daily dosage is 120 mg.

SUMM Great efforts have been made in the 1990's to enrich the active therapeutic components of **Ginkgo biloba** extract and to reduce its content of ginkgolic acids. At the same time, possibilities have been exploited to provide specific combinations of the effective components of **Ginkgo biloba** extract

L16 ANSWER 40 OF 60 USPATFULL on STN
ACCESSION NUMBER: 2001:116602 USPATFULL
TITLE: Compositions for treating alzheimer's disease and other amyloidoses
INVENTOR(S): Castillo, Gerardo, Seattle, WA, United States
Snow, Alan D., Lynnwood, WA, United States
DeSantis, Deborah A., Coral Springs, FL, United States
PATENT ASSIGNEE(S): University of Washington, Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6264994	B1	20010724
APPLICATION INFO.:	US 1998-208278		19981208 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1998-79829, filed on 15 May 1998		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-46602P	19970515 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Prats, Francisco
ASSISTANT EXAMINER: Coe, Susan
LEGAL REPRESENTATIVE: Dwyer, Patrick M.
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 10 Drawing Page(s)
LINE COUNT: 2354
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A composition of plant matter comprising Uncaria tomentosa and at least one of **ginkgo biloba**, rosemary, gotu kola and bacopin.

SUMM . . . emulsions, solutions, syrups, tea bags, aerosols (as a solid or in a liquid medium), suppositories, sterile injectable solutions, sterile packaged **powders**, bark bundles and/orbark **powder** which contain Uncaria tomentosa to treat patients with Alzheimer's disease, type II diabetes and other amyloidoses.

SUMM . . . of some standard techniques known to those skilled in the art, including, but not limited to, thin layer chromatography using silica-**coated** plates, and separation and isolation using high pressure liquid chromatography (HPLC). Unknown active ingredients within Uncaria tomentosa found to be. . .

SUMM . . . emulsions, solutions, syrups, tea bags, aerosols (as a solid or in a liquid medium), suppositories, sterile injectable solutions, sterile packaged **powders**, bark bundles and/or bark **powder**] for inhibition of amyloid formation, deposition, accumulation, and/or persistence, regardless of its clinical setting.

SUMM . . . and plant matter from at least one plant selected from the group of plants consisting of, and commonly known as, **ginkgo biloba**, rosemary, gotu kola and bacopin.

SUMM . . . and plant matter from at least one plant selected from the group of plants consisting of, and commonly known as, **ginkgo biloba**, rosemary, gotu kola and bacopin.

SUMM . . . and plant matter from at least one plant selected from the group of plants consisting of, and commonly known as, **ginkgo**

biloba, rosemary, gotu kola and bacopin.

SUMM . . . and plant matter from at least one plant selected from the group of plants consisting of, and commonly known as, **ginkgo biloba**, rosemary, gotu kola and bacopin.

SUMM . . . of both Alzheimer's disease, type II diabetes and other amyloidoses. Uncaria tomentosa extracted from different commercial sources (extracts isolated from gelatin-**coated** capsules, caplets or liquid form) were all found to serve as potent inhibitors of Alzheimer's disease amyloid fibrillogenesis.

SUMM . . . emulsions, solutions, syrups, tea bags, aerosols (as a solid or in a liquid medium), suppositories, sterile injectable solutions, sterile packaged **powders**, bark bundles and/or bark **powder**, using the method employing some or all of the following steps:

SUMM . . . e) precipitation of the active ingredients using an organic solvent such as petroleum ether followed by centrifugation, f) re-dissolving the **pellet** obtained in an organic solvent such as propanol, g) applying to a silica column equilibrated with propanol/10% acetic acid and. . . i) precipitation of the active components using an organic solvent such as petroleum ether, followed by centrifugation, j) re-dissolving the **pellet** obtained in acetonitrile/water/acetic acid, and k) injecting and separation by HPLC, l) identifying amyloid inhibitory ingredients by testing in relevant.

.

SUMM . . . emulsions, solutions, syrups, tea bags, aerosols (as a solid or in a liquid medium), suppositories, sterile injectable solutions, sterile packaged **powders**, bark bundles or bark **powder**

.

SUMM . . . and plant matter from at least one plant selected from the group of plants consisting of, and commonly known as, **ginkgo biloba**, rosemary, gotu kola and bacopin has the ability to inhibit the formation and growth of brain amyloid deposits in subjects.

. .

SUMM . . . emulsions, solutions, syrups, tea bags, aerosols (as a solid or in a liquid medium), suppositories, sterile injectable solutions, sterile packaged **powders**, bark bundles and/or bark **powder**, which contain Uncaria tomentosa, extracts or

L16 ANSWER 36 OF 60 USPATFULL on STN
ACCESSION NUMBER: 2001:237515 USPATFULL
TITLE: **Ginkgo biloba** composition, method to prepare the same and uses thereof
INVENTOR(S): Xie, De Long, Shanghai, China
Wang, Ning, Shanghai, China
Gao, Qi, Shanghai, China
Zhang, Guo An, Shanghai, China
Shao, Bao Ping, Shanghai, China
Jin, Xiao Wu, Shanghai, China
Huang, Xin Sheng, Shanghai, China

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001055629	A1	20011227
	US 6475534	B2	20021105
APPLICATION INFO.:	US 2001-768678	A1	20010124 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-97058, filed on 12 Jun 1998, GRANTED, Pat. No. US 6187314 Continuation of Ser. No. US 1998-44551, filed on 19 Mar 1998, GRANTED, Pat. No. US 6030621
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Albert Wai-Kit Chan, Suite 7803, 1 World Trade Center, New York, NY, 10048
NUMBER OF CLAIMS: 64
EXEMPLARY CLAIM: 1
LINE COUNT: 1656
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI **Ginkgo biloba** composition, method to prepare the same and uses thereof

AB This invention provides different compositions extracted from **Ginkgo biloba** leaves. Said compositions comprise new active components. This invention also provides a method of preparation of the compositions and individual. . .

SUMM [0002] **Ginkgo Biloba** is the oldest genus among existing seed plants and the only survivor of the family Ginkgoaceae, that can be traced back more than 200 million years to the fossils of the Permian period. Preparations of **Ginkgo Biloba** leaves have been used as remedies in China for more than 5,000 years, I.e. since the earliest origin of Chinese herbal medicine. Phytopharmaceutical extracts from the leaves of **Ginkgo biloba** have been applied to treat cerebrovascular and peripheral vascular diseases in many countries, such as Germany, France, Japan and Korea. . .

SUMM [0003] The principal effective component in **Ginkgo biloba** leaves is flavonoids, that comprise at least 14 different compounds, such as flavonols, flavones, flavanols and biflavonoids etc. Among all. . . flavone glycosides and flavonol glycosides, that include kaempferol, quercetin and isorhamnetin with glucose or rhamnose, are the most emphasized in **Ginkgo biloba** extracts on the market for therapeutic purposes (Tebonin.RTM., Tanakan.RTM., Roekan.RTM., or "EGb 761"). As experiments have demonstrated, flavone glycosides and. . . Vol. 15 (1986), 1475-1479; J. Robak et al., Biochem Pharmacol Vol 37 (1988), 837-841 and J. Kleijnen and P.

Knipschild, **Ginkgo biloba** (Drug Profiles), the Lancet 340:1136 (1992). In addition, the flavone glycosides and flavonol glycosides increase peripheral circulation. Methods of preparation of **Ginkgo biloba** extracts with a greatly enriched content of flavone glycosides as the active components are described in DE-B 17 67 098 and DE-B 21 17 429. These preparations are **Ginkgo biloba** monoextracts.

SUMM [0004] Besides flavonoids, another major active constituent in **Ginkgo biloba** leaves is terpene lactones, that include ginkgolides A, B, C, J, M and bilobalide. Ginkgolides are terpenoid substances with lactone. . .

SUMM [0006] In addition to the compounds mentioned above, **Ginkgo biloba** leaves also contain at least 12 alkyl phenolic acid compounds including ginkgolic acids (anacardic acids) that are 6-alkylsalicylic acids with. . . (1968), 739-743. Structurally similar to the irritants in poison ivy, ginkgolic acids are the factors responsible for toxic effects of **Ginkgo biloba** extracts, that include gastrointestinal disturbances, headaches, skin irritation, dermatitis and edema. Many cases of allergic reactions after contact with **Ginkgo biloba** leaves or fruits have been reported since the 1960's; see G. A. Hill et al., J. Am. Chem. Soc., Vol.. . .

SUMM [0007] **Ginkgo biloba** extract used most frequently at present for therapeutic purposes (Tebonin.RTM., Tanakan.RTM., Roekan.RTM., or "EGb 76111") contains 24% flavone glycosides and. . . the ginkgolides A, B, C and J as well as the bilobalide, which makes up approximately half of the 6%. **Ginkgo biloba** extract

L16 ANSWER 35 OF 60 USPATFULL on STN
ACCESSION NUMBER: 2002:13806 USPATFULL
TITLE: Microencapsulated and controlled-release herbal formulations
INVENTOR(S): Blatt, Yoav, Rehovot, ISRAEL
Kimmelman, Eugene, Rehovot, ISRAEL
Cohen, David, Petach Tikva, ISRAEL
Rotman, Avner, Rehovot, ISRAEL
PATENT ASSIGNEE(S): Bio Dar Ltd., Yavne, ISRAEL (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6340478	B1	20020122	
APPLICATION INFO.:	US 1999-327752		19990607	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Pulliam, Amy E
LEGAL REPRESENTATIVE: Abelman, Frayne & Schwab
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 543
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM **Powdered** and granulated herbal (botanical) extracts and dried, ground dry plants are good and well accepted sources of certain bioactive compounds.

SUMM In the context of the present description and claims, the term "granulated herb" will be understood to refer to both **powdered** and granulated forms of both herbal extracts and herbal plants or portions of herbal plants, which extracts, plants or portions thereof have been ground to a **particle** size within the range of about 100 to about 2000 .mu.m diameter, preferably in the range of about 300 to. . .

SUMM In another preferred embodiment of the invention, the formulation comprises granulated herbs mixed or **coated** with an adjuvant or mixture of adjuvants selected from the group consisting of synthetic polyvinyl-type polymers, synthetic polyethylene-type polymers, cellulose-type. . .

SUMM In one preferred embodiment of the invention, the process is characterized in that the granulated herb is (i) mixed or **coated** with an adjuvant or mixture of adjuvants selected from the group consisting of synthetic polyvinyl-type polymers, synthetic polyethylene-type polymers, cellulose-type. . .

SUMM In another preferred embodiment of the invention, the process is characterized in that the granulated herb is (i) mixed or **coated** with an adjuvant or mixture of adjuvants selected from the group consisting of synthetic polyvinyl-type polymers, synthetic polyethylene-type polymers, cellulose-type. . . polyacrylate-type polymers, fats, waxes and sugars , (ii) then processed into a form selected from the group of microcapsules and **pellets**, and (iii) the microcapsules or **pellets** are filled into hard gelatin capsules.

SUMM In a preferred embodiment of the invention, the process is characterized in that the granulated herb is (i) mixed or **coated** with an adjuvant or mixture of adjuvants selected from the group consisting of synthetic polyvinyl-type polymers, synthetic polyethylene-type polymers,

cellulose-type. . . synthetic polyacrylate-type polymers, fats, waxes and sugars, (ii) then processed into a form selected from the group of microcapsules and **pellets**, and (iii) said microcapsules or **pellets** are compressed into tablets.

SUMM . . . accordance with a preferred embodiment of the invention an orally-administrable formulation for the controlled release of a granulated herb, comprising **particles** of granulated herb **coated** with a film comprising a mixture of at least one water soluble polymer and at least one water insoluble polymer,. . . substantially zero order linear release pattern of at least one active ingredient. In one preferred embodiment of the invention, the **particles** comprise **particles** which are non-spherically shaped. In another preferred embodiment of the invention, the **particles** comprise **particles** which are spherically shaped.

SUMM . . . accordance with a preferred embodiment of the invention an orally-administrable formulation for the controlled release of a granulated herb, comprising **particles** of granulated herb **coated** with an enteric **coating** comprising a polymer film comprising a polymer which is insoluble at a pH below about 5.5. In

L16 ANSWER 18 OF 60 USPATFULL on STN
ACCESSION NUMBER: 2003:268064 USPATFULL
TITLE: Method of treating dermatological disorders with fruit extracts
INVENTOR(S): Murad, Howard, 4265 Marina City Dr. Penthouse 11, Marina del Rey, CA, United States 90292

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6630163	B1	20031007
APPLICATION INFO.:	US 2000-501218		20000210 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-130713P	19990422 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Di Nola-Baron, Liliana
LEGAL REPRESENTATIVE: Pennie & Edmonds LLP
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1961

SUMM . . . and herb extracts to allegedly protect the body against free radicals. In particular, the PYCNOGENOL.RTM. COMPLEX.TM. contains pycnogenol, proanthodyn, quercetin, **Ginkgo Biloba** extract, Green Tea extract, Bilberry extract, Silymarin, Tumeric extract, Hawthorn Berry extract, Rosemary extract, vitamin C (in the form of. . .

SUMM . . . echinacea extract, golden seal, or a mixture thereof. The antioxidant may be a catechin-based preparation, a vitamin A source, a **ginko biloba** extract, a silymarin source, a quercetin compound, a vitamin C source, a carotenoid, or a mixture thereof. The one or. . .

SUMM . . . potato, rice, wheat), pregelatinized starch, gelatin, sucrose, acacia, alginic acid, sodium alginate, guar gum, ethyl cellulose, carboxymethylcellulose sodium, carboxymethylcellulose calcium, **polyvinylpyrrolidone**, methylcellulose, hydroxyproply methylcellulose, microcrystalline cellulose, polyethylene glycol, **powdered** cellulose, glucose, croscarmellose sodium, crospovidone, polacrilin potassium, sodium starch glycolate, tragacanth, calcium carbonate, dibasic calcium phosphate, tribasic calcium phosphate, kaolin,. . .

SUMM . . . carotenoids, echinacoside and caffeoyl derivatives, oligomeric proanthocyanidins or proanthanols (e.g., grape seed extract), silymarin (e.g., milk thistle extract, Silybum marianum), **ginkgo biloba**, green tea polyphenols, and the like, and mixtures thereof. Indeed, any pharmaceutically acceptable compounds suitable for administration orally or topically. . .

SUMM The composition may also include quercetin **powder** as an additional antioxidant. Preferably, the quercetin **powder** is quercetin dihydrate. When included in the composition, the quercetin is typically present in an amount from about 1 to. . .

SUMM In another embodiment, **Ginkgo Biloba** extract is optionally included in the composition. Volatile oils, tannin and resin are believed to be the active constituents of the extract. **Ginkgo Biloba** supplies antioxidants that are believed

to target the brain. **Ginkgo Biloba**, when used in the composition, is typically present in an amount from about 0.01 to 3 weight percent, preferably from. . .

SUMM . . . cellulose, diluents, granulating agents, lubricants, binders, disintegrating agents, and the like. In the case of oral solid preparations (such as **powders**, capsules, and tablets), the oral solid preparations are typically preferred over the oral liquid preparations.

SUMM . . . may be presented as discrete units including aerosol sprays, each containing a predetermined amount of the active ingredient, as a **powder**, stick, or **granules**, as creams (e.g., a conditioner), pastes, gels, lotions (e.g., a sunscreen), syrups, or ointments, on sponges or cotton applicators, or. . .

SUMM . . . such as capsules, cachets, or tablets, or aerosol sprays, each containing a predetermined amount of the active ingredient, as a **powder** or **granules**, as creams, pastes, gels, or ointments, or as a solution or a suspension in an aqueous liquid, a non-aqueous liquid,. . .

SUMM . . . Compressed tablets may be prepared by compressing in a suitable machine the active ingredient in a free-flowing form such as **powder** or **granules**, optionally mixed with a binder, lubricant, inert diluent, surface active or dispersing agent. Molded tablets may be made by molding, in a suitable machine, a mixture of the **powdered** compound moistened with an inert liquid diluent. Desirably, each tablet, cachet or capsule contains from about 1 mg to 2,000. . .

SUMM . . . capsules, and gel caps are preferred, in which case solid pharmaceutical carriers may be employed. If desired, tablets may be **coated** by standard aqueous or non-aqueous techniques.

DETD . . . Extract/ 0.01-3.0
Granatum) Extract Nutritional Science Int'l
Part C Alcohol Denat. SD ALCOHOL 40-B, 1.0-15.0
Anhydrous/Remet
Salicylic Acid Salicylic Acid, **powder**, 0.5-2.0
U.S.P./N.F./Spectrum
Part D PPG-5-Ceteth-20 PROCETYL AWS/Croda 0.5-2.0
Retinyl Palmitate Vitamin A Palmitate, 0.01-0.1
type P1.7/Roche
Linoleic Acid EMERSOL 315/Henkel. . .
#A11513/779350/
Haarmann & Reimer
Part E Glycolic Acid GLYPURE 70% 1.0-10.0
Glycolic Acid/

L16 ANSWER 59 OF 60 USPATFULL on STN

ACCESSION NUMBER:	95:24696 USPATFULL
TITLE:	Extract from **Ginkgo biloba** leaves, its method of preparation and pharmaceuticals containing the extract
INVENTOR(S):	Schwabe, Klaus-Peter, Karlsruhe, Germany, Federal Republic of
PATENT ASSIGNEE(S):	Dr. Willmar Schwabe GmbH & Co., Karlsruhe, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5399348		19950321
APPLICATION INFO.:	US 1992-905167		19920624 (7)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1990-625729, filed on 4 Dec 1990, now abandoned		

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1989-39400913	19891204

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Wityshyn, Michael G.
ASSISTANT EXAMINER:	Gitomer, Ralph
LEGAL REPRESENTATIVE:	Kenyon & Kenyon
NUMBER OF CLAIMS:	16
EXEMPLARY CLAIM:	7
LINE COUNT:	446

TI Extract from **Ginkgo biloba** leaves, its method of preparation and pharmaceuticals containing the extract

AB The invention relates to an improved extract from **Ginkgo biloba** leaves, a method of preparation of the same and pharmaceuticals containing the extract.

SUMM The invention relates to an improved extract from **Ginkgo biloba** leaves, a method of preparation of the extract and the

L16 ANSWER 58 OF 60 USPATFULL on STN
ACCESSION NUMBER: 95:27070 USPATFULL
TITLE: **Pellets** containing plant extracts, process of making same and their pharmaceutical peroral or cosmetic use
INVENTOR(S): Wunderlich, Jens-Christian, Heidelberg, Germany, Federal Republic of
Schick, Ursula, Wiesloch, Germany, Federal Republic of
Freidenreich, Jurgen, Schriesheim, Germany, Federal Republic of
Werry, Jurgen, Ludwigshafen, Germany, Federal Republic of
PATENT ASSIGNEE(S): ALFATEC Pharma GmbH, Heidelberg, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5401502		19950328	
APPLICATION INFO.:	US 1992-876866		19920430	(7)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1992-42011795	19920117

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Kulkosky, Peter F.
LEGAL REPRESENTATIVE: Behr, Omri M., McDonald, Matthew J.
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 837
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI **Pellets** containing plant extracts, process of making same and their pharmaceutical peroral or cosmetic use

AB Plant extract containing **pellets** are formed by a dispersion of plant extract or extracts in a matrix, principally comprising a skeleton builder namely collagen,. . . the skeleton former and the plant extract dropped into a very cold inert fluid, suitably liquid nitrogen, to form the **pellets** and the thus formed **pellets** dried.

SUMM The present invention concerns **pellets**, that is to say, spheres containing plant extract or extracts characterized thereby that the plant extract dispersed in a matrix. . .

SUMM The invention is further concerned with a protective process for the preparation of such **pellets** or solid spheres, which may be utilized for pharmaceutical, oral, or cosmetic purposes.

SUMM This task is solved by the present Invention by producing plant extract containing **pellets** characterized by a dispersion of plant extracts in a matrix whose skeleton principally consists of a hydrophilic macromolecule.

SUMM The task is further solved by a process for the preparation of such plant extract containing **pellets** characterized thereby that the skeleton forming material in solid or dissolved form is mixed with or emulsified with, for example, solid extract in a solution of the skeleton former, or suspended and formed into molded **particles**. The molded **particles** may, if necessary, be dried. Care should be taken however that no incompatibilities of the matrix system

or the active. . .

SUMM In particular, the present invention makes available molfed **particles** containing plant extract characterized by a dispersion of the plant extract in a matrix which comprises principally a skeleton former. . .

SUMM Furthermore, the present invention makes available a process for the formation of plant extract containing molded **particles** characterized thereby that

SUMM . . . obtained mixture of skeleton former and plant extract is dropped into an exceedingly cold inert fluid to form molded body **particles**.

L16 ANSWER 56 OF 60 USPATFULL on STN

ACCESSION NUMBER: 96:108681 USPATFULL

TITLE: Shaped articles containing plant extract(s), in particular **pellets**, and their pharmaceutical or cosmetic use

INVENTOR(S): Wunderlich, Jens-Christian, Heidelberg, Germany, Federal Republic of
Schick, Ursula, Schriesheim, Germany, Federal Republic of
Werry, Jurgen, Ludwigshafen, Germany, Federal Republic of
Freidenreich, Jurgen, Schriesheim, Germany, Federal Republic of

PATENT ASSIGNEE(S): Alfatec-Pharma GmbH, Heidelberg, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5578307		19961126	
	WO 9313754		19930722	
APPLICATION INFO.:	US 1994-256651		19941018	(8)
	WO 1993-DE37		19930118	
			19941018	PCT 371 date
			19941018	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1992-4201172	19920117

L16 ANSWER 55 OF 60 USPATFULL on STN

ACCESSION NUMBER:	1999:34038 USPATFULL			
TITLE:	Compositions and methods for the control of smoking			
INVENTOR(S):	King, Michael Glenn, 21 Muv 97, Ballarut Victoria, Australia			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5883137		19990316	
	WO 9609042		19960328	
APPLICATION INFO.:	US 1997-809400		19970321	(8)
	WO 1995-AU621		19950921	
			19970321	PCT 371 date
			19970321	PCT 102(e) date
	NUMBER		DATE	
PRIORITY INFORMATION:	AU 1994-8353		19940923	
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	MacMillan, Keith D.			
LEGAL REPRESENTATIVE:	Dann, Dorfman, Herrell and Skillman			
NUMBER OF CLAIMS:	16			

STN

ACCESSION NUMBER:	1999:110362 USPATFULL
TITLE:	Agents acting against hyperreactive and hypoactive, deficient skin conditions and manifest dermatitides
INVENTOR(S):	Lanzendorfer, Ghita, Hamburg, Germany, Federal Republic of Stab, Franz, Echem, Germany, Federal Republic of Untiedt, Sven, Hamburg, Germany, Federal Republic of
PATENT ASSIGNEE(S):	Beiersdorf AG, Hamburg, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5952373		19990914	
	WO 9618381		19960620	
APPLICATION INFO.:	US 1997-849523		19970908	(8)
	WO 1995-EP4907		19951212	
			19970908	PCT 371 date
			19970908	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1994-4444238	19941213

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Weddington, Kevin E.
LEGAL REPRESENTATIVE:	Sprung Kramer Schaefer & Briscoe
NUMBER OF CLAIMS:	4
EXEMPLARY CLAIM:	1
LINE COUNT:	1583

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . of benzoin resin, aqueous or alcoholic tobacco, tea and/or

L16 ANSWER 48 OF 60 USPATFULL on STN

ACCESSION NUMBER:	2000:24295 USPATFULL
TITLE:	**Ginkgo biloba** composition, method to prepare the same and uses thereof
INVENTOR(S):	De Long, Xie, 1271 Dong Fang Rd. Pudong, Shanghai, China Ning, Wang, 1271 Dong Fang Rd. Pudong, Shanghai, China Qi, Gao, 1271 Dong Fang Rd. Pudong, Shanghai, China An, Zhang Guo, 1271 Dong Fang Rd. Pudong, Shanghai, China Ping, Shao Bao, 1271 Dong Fang Rd. Pudong, Shanghai, China Wu, Jin Xiao, 1271 Dong Fang Rd. Pudong, Shanghai, China Sheng, Huang Xin, 1271 Dong Fang Rd. Pudong, Shanghai, China

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6030621		20000229	
APPLICATION INFO.:	US 1998-44551		19980319	(9)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Lankford, Jr., Leon B.
ASSISTANT EXAMINER:	Tate, Christopher R.
LEGAL REPRESENTATIVE:	Elkins, Mark
NUMBER OF CLAIMS:	5
EXEMPLARY CLAIM:	1
LINE COUNT:	1447

CAS INDEXING IS AVAILABLE FOR THIS PATEN

L16 ANSWER 47 OF 60 USPATFULL on STN

ACCESSION NUMBER:	2000:124581 USPATFULL
TITLE:	Method of producing multi-layer medicaments in solid form for oral or rectal administration
INVENTOR(S):	Breitenbach, Jorg, Mannheim, Germany, Federal Republic of Hartl, Axel Paul, Dirmstein, Germany, Federal Republic of Hofmann, Jurgen, Ludwigshafen, Germany, Federal Republic of Rosenberg, Joerg, Ellerstadt, Germany, Federal Republic of Schiessl, Michael, Hassloch, Germany, Federal Republic of Zettler, Hans Dieter, Grunstadt, Germany, Federal Republic of
PATENT ASSIGNEE(S):	BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6120802		20000919	
	WO 9715293		19970501	
APPLICATION INFO.:	US 1998-51544		19980415	(9)
	WO 1996-EP4601		19961023	
			19980415	PCT 371 date
			19980415	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1995-19539361	19951023

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Page, Thurman K.
ASSISTANT EXAMINER:	Howard, S.
LEGAL REPRESENTATIVE:	Keil & Weinkauf
NUMBER OF CLAIMS:	10
EXEMPLARY CLAIM:	1

L16 ANSWER 40 OF 40 USPATFULL on STN

ACCESSION NUMBER:	95:31641 USPATFULL
TITLE:	Means for containing active substances, having a shell of hydrophilic macromolecules, active substances and process for preparation thereof
INVENTOR(S):	Wunderlich, Jens-Christian, Heidelberg, Germany, Federal Republic of Schick, Ursula, Wiesloch, Germany, Federal Republic of Freidenreich, Jurgen, Schriesheim, Germany, Federal Republic of Werry, Jurgen, Ludwigshafen, Germany, Federal Republic of
PATENT ASSIGNEE(S):	Alfatec Pharma GmbH, Heidelberg, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5405616		19950411	
APPLICATION INFO.:	US 1992-876864		19920430	(7)
DISCLAIMER DATE:	20120328			

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1992-42011795	19920117

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Phelan, D. Gabrielle
ASSISTANT EXAMINER:	Kulkosky, Peter F.
LEGAL REPRESENTATIVE:	Behr, Omri M., McDonald, Matthew J.
NUMBER OF CLAIMS:	33
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT:	1138

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . active material and the particular use selected. Thus, for example materials such as dextrans, modified starches, sugar and in particular, **mannitol** containing pellets, are formed which, as lipophilisates form a high porous network. Macromolecules such as alginates, agar agar, and pectin. . .

SUMM . . . traganth, xanthan, natural as well as modified starches, dextrans, dextrins, maltodextrin, chitosin, alginates, alginate calcium phosphate, cellulose derivatives, polyvinyl alcohol, **polyvinylpyrrolidone**, polyacrylic acid, and polymers of methacrylic acid and methacrylic acid esters.

DRWD 41. Phytopharmaceuticals, for example, i.e., **ginkgo biloba** extract;

DETD 250 g. **Mannitol**

CLM What is claimed is:

. . . gum arabic, pectin, tragacanth, xanthan, natural and modified starches, dextrans, dextrins, maltodextrin, chitosan, alginates, cellulose derivatives, dextran, sugar, glycine, lactose, **mannitol**, polyvinyl pyrrolidone, polyacrylic acid, polymers of methacrylic acid, polymers of methacrylic acid esters and mixtures thereof said additional skeleton forming. . .

IT 50-70-4, Sorbitol, biological studies 56-40-6, Glycine, biological studies 63-42-3, Lactose **69-65-8**, D-Mannitol **9003-39-8**, PVP 9004-54-0, Dextran, biological studies

(pellets contg. dihydropyridine deriv. drug and)

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jan  9, 2004 (20040109/UP).

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L16 ANSWER 39 OF 40 USPATFULL on STN

ACCESSION NUMBER: 96:108681 USPATFULL

TITLE: Shaped articles containing plant extract(s), in particular pellets, and their pharmaceutical or cosmetic use

INVENTOR(S): Wunderlich, Jens-Christian, Heidelberg, Germany, Federal Republic of
Schick, Ursula, Schriesheim, Germany, Federal Republic of
Werry, Jurgen, Ludwigshafen, Germany, Federal Republic of
Freidenreich, Jurgen, Schriesheim, Germany, Federal Republic of

PATENT ASSIGNEE(S): Alfatec-Pharma GmbH, Heidelberg, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5578307		19961126	
	WO 9313754		19930722	
APPLICATION INFO.:	US 1994-256651		19941018	(8)
	WO 1993-DE37		19930118	
			19941018	PCT 371 date
			19941018	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1992-4201172	19920117
	DE 1992-4201179	19920117

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rollins, John W.
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis
NUMBER OF CLAIMS: 37
EXEMPLARY CLAIM: 1
LINE COUNT: 1079
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . plant extracts or of extracts or individual substances obtained therefrom: Flavonoids and their aglycones: rutin, quercetin, diosmin, hyperoside, (neo)hesperidin, hesperitin, **Ginkgo biloba** (for example ginkgo flavone glycosides), Crataegus extract (for example oligomeric procyanidines), buckwheat (for example rutin), Sophora japonica (for example rutin),. . .

SUMM . . . consisting of: albumin, agar-agar, gum arabic, pectins, tragacanth, xanthan, natural and modified starches, dextrans, dextrins, maltodextrin, chitosan, alginates, cellulose derivatives, **polyvinylpyrrolidone**, dextran, sugars, glycine, lactose, **mannitol**, polyacrylic acid, methacrylic acid polymers, methacrylate polymers, and their mixtures may be added at a concentration of 1-50%.

SUMM . . . xanthan, natural and modified starches, dextrans, dextrins, maltodextrin, chitosan, alginates, cellulose derivatives, sugars, such as, for example, sucrose, glycine, lactose, **PVP** (**polyvinylpyrrolidone**), **mannitol** and combinations of the abovementioned substances, but in particular **mannitol**.

SUMM . . . dissolution characteristics of the polymeric skeleton to suit

L17 ANSWER 7 OF 33 USPATFULL on STN
ACCESSION NUMBER: 2003:203149 USPATFULL
TITLE: Modified release multiple-units compositions of non-steroid anti-inflammatory drug substances (NSAIDs)
INVENTOR(S): Skinh.o slashed.j, Annette, R.o slashed.dovre, DENMARK
Bertelsen, Poul, Vanlase, DENMARK
PATENT ASSIGNEE(S): Nycomed Danmark A/S, Roskilde, DENMARK (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6599529	B1	20030729	
	WO 9912524		19990318	
APPLICATION INFO.:	US 2000-508594		20000717	(9)
	WO 1998-DK388		19980910	

	NUMBER	DATE
PRIORITY INFORMATION:	DK 1997-1044	19970911

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Spear, James M.
ASSISTANT EXAMINER: Di Nola-Baron, Liliana
LEGAL REPRESENTATIVE: Corless, Peter F., O'Day, Christine C., Edwards & Angell, LLP
NUMBER OF CLAIMS: 51
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 2701
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . to enable a delayed and extended release of the drug substance.

Typically, the second fraction comprises multiple units which are **coated** with a sustained release **coating** designed to release the drug substance in such a manner that the maintenance of a therapeutically active plasma concentration for. . .

SUMM . . . a sustained release opioid formulation comprising a plurality of substrates comprising the active ingredient in a sustained release matrix or **coated** with a sustained release **coating** comprising a retardant material. The sustained release beads are then **coated** with an opioid in immediate release form or, in the case the composition is in the form of a gelatine. . . via inclusion of a sufficient amount of opioid within the capsule. In a further alternative, the gelatine capsule itself is **coated** with an immediate release layer of the opioid.

SUMM . . . disintegration time in water of at the most about 15 min for uncoated tablets, cf. Ph. Eur. (the requirements for **coated** tablets or capsules are at the most 30 min), ii) a traditionally formulated granulate or iii) loose powder of the. . .

SUMM . . . reliable. The composition should also be very storage stable because an immediate release due to accidental damaging of e.g. the **coating** or capsule of a high dosage form may result in undesired high plasma concentrations, so-called dose dumping, which could cause. . .

SUMM By use of a **coated** multiple unit dosage form, the risk of dose dumping due to e.g. rupturing of a **coating** is reduced because the amount of active ingredient in each **coated** unit is

negligible.

SUMM the second fraction being in the form of **coated** delayed release multiple-units for extended release of the NSAID substance.

SUMM a second fraction of **coated** modified release multiple-units for extended release in vivo of an NSAID substance to maintain a therapeutically and/or prophylactically active plasma. . .

SUMM . . . (cf. Danish Patent Application filed on Sep. 10, 1998 in the name of Nycomed Danmark). In those cases, where a **coating** is present on the units of the first fraction, the **coating** may of course also contribute to the control of the release of the active drug substance from the first fraction.. . .

SUMM . . . believed to be associated with high blood levels of NSAID substances. Furthermore, the delayed or extended release properties of the **coating** applied on the second fraction of the multiple-units dosage forms of the present invention are unaffected by the pH in. . .

SUMM The first fraction of the multiple-units dosage form of the invention may also be in the form of **coated** multiple-units provided that the release rate of such a fraction is so fast in the dissolution medium employed in dissolution. . .

SUMM When a **coating** is present on the multiple-units of the first fraction then it could advantageous be of the same kind as an outer **coating** on the multiple-units of the second fraction. The employment of the same kind of **coating** for each fraction may be performed with substantially identical procedures and materials and the production cost can be kept at. . .

SUMM the second fraction being in the form of **coated** delayed release multiple units for extended release of the NSAID substance..

SUMM . . . fast or quick release fraction (i.e. the first fraction) and an extended or slow release fraction (i.e. the second fraction, **coated** pellets). The estimated in vivo dissolution profile for the once daily composition can be used as the target in vitro. . .

SUMM . . . amount of the active substance within the first 20 min or 1 hours under acidic conditions, then the controlled release **coating** is not necessarily designed as an enteric **coating**, i.e. a **coating** which is insoluble at acidic pH and soluble at neutral/basic pH. The compositions according to the invention exemplified in the experimental section are examples on compositions wherein the controlled release **coating** of the second fractions is not an enteric **coating**. Furthermore, application of an enteric **coating** on e.g. pellets would not lead to an extended release of an active drug substance. The release will of course be delayed (no release under acidic conditions) but as the pH becomes neutral and alkaline, then the enteric **coating** dissolves, i.e. there is no membrane left to control the release.

SUMM In a preferred embodiment, the multiple units of the second and, when appropriate, the first fraction are **coated**, cross-sectionally substantially homogeneous pellets.

SUMM As discussed above, the multiple-units of the first fraction may be in the form of uncoated pellet cores, **coated** pellet cores, granules, a granulate or small plain tablets provided that the requirements with respect to release of active drug. . . described under dissolution method II herein are fulfilled. In those cases, where the first fraction is in the form of **coated** pellets, the time lag of the release from the second fraction relative to the first fraction may be obtained by a modified release **coating** of the

second fraction which is present in a range of about 2%-80% such as, e.g., about 2%-70%, about 2-60%,. . .

SUMM It is also preferred that the modified release **coating** of the fraction(s) is substantially water-insoluble, but water-diffusible and substantially pH-independent which will facilitate an absorption independent of the presence. . .

SUMM . . . obtain a therapeutically or prophylactically active plasma concentration within a relatively short period of time, and a second fraction of **coated** extended release multiple-units for extended release in vivo of an NSAID substance to maintain a therapeutically active plasma concentration in. . .

SUMM The term modified release in the present context refers to a composition which can be **coated** or uncoated and prepared by using pharmaceutically acceptable excipients and/or specific procedures which separately or together are designed to modify. . .

SUMM . . . composition, the present inventors have found that the first fraction should be in the form of uncoated multiple-units as the **coating** or the manufacture of the units to a form suitable for application of a **coating** seem to have a retarding effect on the release rate of the active drug substance from the first fraction (see. . . very low solubility in this medium. First fractions containing such active drug substances are generally not in the form of **coated** multiple-units in compositions according to the invention (cf. the discussion above).

SUMM . . . 5.0 such as at least about 5.5 the multiple-units of the invention may as well be in the form of **coated** multiple-units such as, e.g., **coated** pellet cores.

SUMM The first fraction may be **coated** when the NSAID substance has a solubility in 0.1 N hydrochloric acid at room temperature of at least about 0.1%. . .

SUMM . . . clomipramine hydrochloride, d-phenylalanine, demexiptiline, demexiptiline hydrochloride, dimethacrine tartrate, dothiepin, dothiepin hydrochloride, doxepin, fluphenazine hydrochloride, fluvoxamine, fluvoxamine hydrogen maleate, fluvoxamine maleate, **ginkgo biloba**, indalpine, isocarboxazide, johanniskrauttrockenestrakt, l-tryptophan, lithium citrate, lithium sulfate, lofepramine, maprotiline, maprotiline hydrochloride, maprotiline mesilate, medifoxamine, metaprimine fumarate, mianserin, moclobemide, nitroxazepine. . .

SUMM As described above, the first fraction may also be in the form of **coated** multiple-units such as **coated** pellets provided that the pK, of the active drug substance is at least about 5.0 or 5.5. From the experimental section inter alia it appears that such **coated** cores may have the same **coating** as the **coating** of the second fraction, but the thickness of the **coating** differs in such a manner that the **coating** of the first fraction is much thinner than that of the second fraction. For further details with respect to **coating** see below.

SUMM When the pellets or beads are not **coated**, the combination of the active substance and the excipients is referred to as a core.

SUMM . . . reproducible release of the active ingredient than compared to e.g. particles in which the active ingredient forms part of the **coating**.

SUMM . . . release profile of the core of the individual unit is substantially non-limiting with respect to the desired release of the

coated pellet, e.g. that the core itself provides at least about 90% w/w such as, e.g., at least about 95% w/w,. . .

SUMM **Coating**

SUMM a) individual units containing an active substance are **coated** with an inner film-**coating** mixture ("the inner **coat** ") comprising a film-forming substance,

SUMM b) the thus **coated** units are optionally provided with a first outer film layer comprising e.g. a stabilizing agent ("the middle **coat**"),

SUMM c) the thus **coated** units of the second fraction are optionally provided with a second outer film layer comprising a film-forming agent ("the outer **coat**"),

SUMM In general, the inner **coating** is applied in an amount corrsponding to 2-20% w/w. The middle **coating**, if present, is applied in an amount corresponding to about 4% w/w of the uncoated units

and the outer **coat** is applied in an amount corresponding to about 1-2% w/w of the uncoated units.

SUMM . . . film-forming agent of step c) may be so selected that adhesion between the units is prevented at elevated temperatures, the **coated** units are then subsequently heated to a temperature above 40.degree. C., preferably not above 65-75.degree. C., and thereby a continuous. . . in homogeneous admixture with the film-forming substance. In some cases, this curing process may also take place before

the outer **coating** layer may be applied.

SUMM The modified release **coating** is applied on the multiple units from a solution and/or suspension preferably in an aqueous solvent, but an organic **coating** composition may also be applied.

SUMM In one preferred embodiment, the acrylic **coating** is an acrylic resin lacquer used in the form of an aqueous dispersion, such as that which is commercially available from Rohm Pharma under the tradename Eudragit.RTM.. In further preferred embodiments, the acrylic **coating** comprises a mixture of two acrylic resin lacquers commercially available from Rohm Pharma under the tradenames Eudragit.RTM. RL 30 D. . . D and 1:40 in Eudragit.RTM. RS 30 D. Eudragit.RTM. RL/RS mixtures are insoluble in water and in digestive fluids. However, **coatings** formed from the same are swellable and permeable in aqueous solutions and digestive fluids. The Eudragit.RTM. RL/RS dispersions may be. . . modified release formulation having a desirable dissolution profile. The most desirable modified release formulations may be obtained from a retardant **coating** based on Eudragit.RTM. NE 30 D, which is a neutral resin having a molecular weight of 800,000.

SUMM The amount of **coating** applied is adapted so as to obtain a predetermined dissolution characteristic of the fraction of the composition. The percentage by weight of the modified release **coating** on the individual pellet will, for the fraction providing the extended duration of effect of the NSAID substance, be at.

. . about 3% to 6% w/w on an average, based on the weight of the uncoated individual pellet. The amount of **coating** applied depends on the predetermined dissolution characteristics of the particular core composition and the desired release profile of the fraction.

SUMM However, the amount of **coating** applied should also be adapted so that there will be no rupturing problems.

SUMM The **coating** may be admixed with various excipients such as

plasticizers, anti-adhesives such as, e.g., colloidal silicium dioxide, inert fillers, and pigments. . .

SUMM Tackiness of the water-dispersible film-forming substances may be overcome by simply incorporating an anti-adhesive in the **coating** . The anti-adhesive is preferably a finely divided, substantially insoluble, pharmaceutically acceptable non-wetting powder having anti-adhesive properties in the **coating**. Examples of anti-adhesives are metallic stearates such as magnesium stearate or calcium stearate, microcrystalline cellulose, or mineral substances such

as. . . potassium silicates and talc. The preferred anti-adhesive is talc. The anti-adhesive or mixture of anti-adhesives is preferably incorporated in the **coating** in an amount of about 0.1-70% by weight, in particular about 1-60% by weight, and preferably about 8-50% by weight. . .

SUMM The individual modified release **coated** multiple-units may further comprise a middle **coating** between the "inner **coat**" and the "outer **coat**". Such **coating** may be adapted to stabilize the controlled release **coated** multiple-units and to prevent undesired changes of the release profile of each **coated** unit. Accordingly, the middle lacquer or **coating** may contribute to stability of the release profile of the dosage unit. Accordingly, the multiple units may further comprise an. . .

SUMM . . . about 50.degree. C., such as a temperature between about 60.degree. C. and about 120.degree. C., and being selected from diffusion **coating** materials such as ethylcellulose or enteric **coating** materials such as anionic poly(meth)acrylic acid esters, hydroxypropylmethylcellulosephthalate, celluloseacetatephthalate, polyvinylacetatephthalate, polyvinylacetate phthalate-crotonic acid copolymerisates, or mixtures thereof, or water-soluble **coating** materials such as water-soluble cellulose derivatives, e.g. hydroxypropylcellulose, carboxymethylcellulose, methylcellulose, propylcellulose, hydroxyethylcellulose, carboxyethylcellulose, carboxymethylhydroxyethylcellulose, hydroxymethylcellulose, carboxymethylethylcellulose, methylhydroxypropylcellulose or hydroxypropylmethylcellulose.

SUMM . . . is normally incorporated in an amount of less than 10% by weight, calculated on the dry matter content of the **coating** composition.

SUMM Filler/diluents/binders may be incorporated such as sucrose, sorbitol, **mannitol**, lactose (e.g., spray-dried lactose, .alpha.-lactose, .beta.-lactose, Tablettose.RTM., various grades of Pharmatose.RTM., Microtose or Fast-Floc.RTM.), microcrystalline cellulose (e.g., various grades of. . .

SUMM . . . 31, LH30); starches, including potato starch; croscarmellose sodium (i.e. cross-linked carboxymethylcellulose sodium salt; e.g. Ac-Di-Sol.RTM.); alginic acid or alginates; insoluble **polyvinylpyrrolidone** (e.g. Polyvidon.RTM. CL, Polyvidon.RTM. CL-M, Kollidon.RTM. CL, Polyplasdone.RTM. XL, Polyplasdone.RTM. XL-10); sodium carboxymethyl starch (e.g. Primogel.RTM. and Explotab.RTM.).

DETD . . . of a quick release granulate, Examples 10-17 illustrate inter alia the influence of the composition of the pellets or the **coat** on the release rate and Example 18 relates to an immediate release composition disclosed in EP-A-0 438 249.

DETD Preparation of Cores Containing Lornoxicam and **Coating** of the Cores with a CR **Coating**

DETD Batch Nos. 04029831 (uncoated pellet cores) and 05029833 (**coated**

pellet cores) were prepared.

DETD Lornoxicam pellet cores were prepared by manufacturing of pellet cores and subsequent **coating** with an inner and an outer **coat**

.

DETD 100 g of these pellet cores were **coated** with an inner **coat** and an outer **coat** in a laboratory size bottom spray fluid bed **coater** with a spray pressure of 1 bar for both the inner **coat** and the outer **coat**. The temperature of the **coating** process was maintained at an inlet temperature of approximately 35.degree. C. to 40.degree. C.

DETD The composition of the **coating** is shown in Table 2:

DETD

TABLE 2

Ingredient Amount (g)

Inner **coat**
Hypromellose (Methocel E prem) 3.25
Magnesium stearate 0.68
Talc 6.07
Eudragit NE 30 D 216
Purified water 274
Outer **coat**
Hypromellose (Methocel E5 prem) 4.0
Talc 4.0
Purified water 96.0

DETD In the **coating** process the following amount of inner and outer **coat** was applied. The amount of dry matter applied calculated in percentage of the pellet core weight also appears from the. . .

DETD Inner **coat**: 35.9 g **coating** solution (corresponding to a dry matter content of approximately 5.5% w/w of the pellet core weight)

DETD Outer **coat**: 12.5 g **coating** solution (corresponding to a dry matter content of approximately 1% w/w of the pellet core weight)

DETD After the application of the **coatings**, the **coated** pellet cores were cured at a bed temperature of approximately 70.degree. C. for 30 min, whereafter the **coated** pellet cores were cooled to a bed temperature below 35.degree. C.

DETD After the **coating**, the **coated** pellet cores are screened through a 1.2 mm screen. Oversized material is discarded.

DETD Preparation of **Coated** Pellet Cores Having a Thinner Inner **Coating** than the **Coated** Pellet Cores of Example 1

DETD Batches Nos 11029831 (uncoated pellet cores) and 20029832 (**coated** pellet cores) were prepared.

DETD The pellet cores were **coated** as described in Example 1 with the exception that in Example 4, 100 g pellet cores were **coated** with an amount of inner and outer **coat** as follows:

DETD Inner **coat**: 20.0 g **coating** solution (corresponding to a dry matter content of approximately 3% w/w of the pellet core weight).

DETD Outer **coat**: 12.5 g **coating** solution (corresponding to a dry matter content of approximately 1% w/w of the pellet core weight).

DETD As appears from the above, the amount of dry matter of the inner **coat** is smaller than in Example 1, whereas the amount of dry

matter of the outer **coat** is the same as in Example 1. Accordingly, it is expected that the release of lornoxicam from the **coated** pellets of Example 4 is faster than that of lornoxicam from the **coated** pellets of Example 1.

DETD Preparation of Pellets **Coated** with a **Coating** Having Varying Amounts of a Hydroxypropylmethylcellulose (HPMC)

DETD In the following, two different batches of **coated** pellets of 100 g each were prepared.

DETD Batch 1 (Batch No. 24029832-**coated** pellet cores):

DETD 100 g pellet cores were **coated** according to the procedure described in Example 1. The composition of the **coating** is as follows:

DETD

Ingredients	Amount (g)
Inner **coat**	
Hypromellose (Methocel E5 prem)	11.3
Magnesium stearate	0.6
Talc	5.4
Eudragit NE 30 D	191.7
Purified water	291
Outer **coat**	
Hypromellose (method E % prem)	4.0
Talc	4.0
Purified water	96.0

DETD The following amount of inner and outer **coat** was used:

DETD Inner **coat**: 20.1 g **coating** solution (corresponding to a dry matter content of approximately 3% wow of the pellet core weight; the HPMC content corresponds. . .

DETD Outer **coat**: 12.5 g **coating** solution (corresponding to a dry matter content of approximately 1% w/w of the pellet core weight).

DETD Batch 2 (Batch No., 26029832-**coated** pellet cores):

DETD 100 g pellet cores were **coated** as described in Example 1. The composition of the **coating** is as follows:

DETD

Ingredients	Amount (g)
Inner **coat**	
Hypromelose (Methocel E5 prem.)	3.74
Magnesium stearate	0.17
Talc	1.48
Eudragit NE 30 D	31.9
Purified water	62.7
Outer **coat**	
Hypromellose (method E % prem)	4.0
Talc	4.0
Purified water	96.0

DETD The following amount of inner and outer **coat** was used:

DETD Inner **coat**: 20.1 g **coating** solution (corresponding to a dry matter content of approximately 3% w/w of the pellet core weight; the HPMC content corresponds. . .

DETD Outer **coat**: 12.5 g **coating** solution (corresponding to a dry matter content of approximately 1% w/w of the pellet core

weight).

DETD . . . it seems as if the fast fraction advantageously may be constituted by a granulate rather than uncoated pellet cores or film-**coated** pellet cores.

DETD Preparation of a Composition Containing a Mixture of Uncoated and **Coated** Pellet Cores

DETD The following example illustrate the dissolution behaviour of a composition containing a mixture of uncoated and **coated** pellet cores. The uncoated pellets are intended to simulate a fast release fraction and the **coated** pellets are intended to simulate a delayed release fraction.

DETD **Coated** pellets obtained according to Example 1 were mixed with pellet cores obtained according to Example 4 and the final composition contained 40% of uncoated pellet cores and 60% **coated** pellets (the percentage is given as % w/w of the total dose of lornoxicam in the composition, i.e. the uncoated fraction accounts for 40% w/w of the total content of lornoxicam whereas the **coated** fraction accounts for 60% w/w of the total content of lornoxicam. A unit dosage form of the composition contains 8. . .

DETD

11029831 (uncoated fraction)` + 05029833 (**coated** fraction) (5.5/4.3).sup.a

Time (h)	Release (% w/w)
0	0
0.5	1.4
1	2.9
2	38.4
3	46.1
4	49.6
5. . .	21 86.4
22	87
23	88.1
24	89

.sup.a(5.5/4.3) relates to the fact that the content of dry matter in the **coat** is 5.5% w/w and the HPML content is 4.3% w/w.

DETD . . . a retardation of the release of lornoxicam is observed at pH 7.4 compared with the uncoated pellets cores, i.e. the **coating** is in control of the release rate. However, a composition containing a mixture of uncoated and **coated** pellets does not seem to enable a fast release of lornoxicam. Therefore, the fast release fraction has to been manipulated. . .

DETD Preparation of a Composition Containing a Mixture of a Quick Release Granulate and a Delayed Release Fraction of **Coated** Pellet Cores

DETD **Coated** pellets obtained according to Example 4 were mixed with a granulate obtained according to Example 9, where the mixture contained. . . form of the granulate and the remaining 60% w/w of the total dose of lornoxicam was in the form of **coated** pellets (the concentration of lornoxicam in the granulate is about 2-3% w/w and about 9% w/w in the uncoated pellets).. . .

DETD

972510 (granulate) + 20029832 (**coated** pellets) (3/4.3)

Time (h)	Release (% w/w)
0	0
1	37.2
2	41.3
3	44.6
4	48.2
5	51.3
6.	. .

DETD . . . to achieve a suitable release even at a low pH. Furthermore, a delayed release is observed with respect to the **coated** pellets fraction.

DETD **Coated** pellets obtained according to Example 8 (batch 1, 15% w/w HPMC in the **coat** was mixed with granulate obtained according to Example 9. The mixture contained 40% w/w of the total dose of lornoxicam in the form of the granulate, whereas the remaining 60% w/w of lornoxicam was in the form of **coated** pellets. The dissolution test was carried out according to dissolution method III. The following dissolution data was obtained:

DETD

972510 (granulate) + 24029832 (**coated** pellets) (3/15.1)

Time (h)	Release (% w/w)
0	0
0.5	35.7
1	35.7
2	43.2
3	50.0
4	55.8
5.	. .

DETD . . . of the delayed release fraction is observed compared with the results obtained in Example 11. Thus, the composition of the **coat** can be adjusted to a suitable release rate. In this example the content of HPMC in the **coat** is 15.1% w/w.

DETD Investigation of the Influence of the Composition of the Controlled Release **Coat** on the Release Rate

DETD **Coated** pellets obtained according to Example 8 (batch 2) were mixed with a granulate obtained according to Example 9. The mixture. . . w/w of the lornoxicam content in the form of the granulate and the remaining 60% w/w in the form of **coated** pellets. The dissolution test was carried out according to dissolution method III.

DETD

972510 (granulate) + 26029832 (**coated** pellets) (3/25.0)

Time (h)	Release (% w/w)
0	0

0.5 37.3
1 37.3
2 58
3 69.1
4 79.9
5. . .
DETD . . . released whereas only 69.4% w/w was released in Example 12. Thus, the increase of the concentration of HPMC in the **coat** (25% in the present example in contrast to 15% in Example 12) has an increasing effect on the release rate. . .
DETD Dissolution data from **coated** pellets from Examples 1, 4 and 8 (batches 1 and 2) were determined by dissolution method I (pH 7.4).
The.
. .
DETD

24029832 26029832
05029833 20029832 (**coated** pellets) (**coated** pellets)
(**coated** pellets) (**coated** pellets) (3.0/15.1) (3.0/25.0)
Time (5.5/4.3) (3.0/4.3) Example 8, Example 8,
(h) Example 1 Example 4 batch 1 batch 2

0 0 0 0. . .
DETD . . . from the composition of Example 1 with that of Example 4 illustrates that the thickness of the CR (controlled release) **coat** influences the release rate in such a manner that a thinner **coat** leads to a more rapid release. The influence of HPMC as an example of a substance which is capable of forming pores in the **coat** on the release rate is illustrated by the release rate of the two different batches of Example 8 and the. . .
DETD Dissolution data from **coated** pellets from Examples 4 and 8 (batch 2) were obtained using dissolution method V (pH 7.3), and are as follows:
DETD

26029832 (**coated**
20029832 (**coated** pellets)
pellets) (3.0/4.3)[7.3] (3.0/25.0)[7.3]
Time (h) Example 4 Example 8, batch 2

0 0 0
0.5 6.2 22
1 10.1 36.1
2 17.3 60.7
3 24.3. . .
DETD Dissolution data from **coated** pellets from Example 4 and Example 8 (batch 2) was determined by dissolution method I (pH 7.4) and method IV. . .
DETD . . . with acid does not have any significantly influence on the rate
of release from the delayed release fraction, i.e. the **coated** pellets fraction.
DETD The results from Examples 15 and 16 have shown that **coated** pellets have the same release rate independent on whether a pre-treatment in acid has been included or not whereas a. . .
CLM What is claimed is: